REMARKS

Claims 30-34 and 90-99 are pending in the application. No claim amendments are presented by way of this reply. Reconsideration of the claims is respectfully requested in view of the following remarks. The Examiner's comments in the Office Action are addressed below in the order set forth therein.

The Rejections of the Claims under 35 U.S.C. §103 Should Be Withdrawn

Claims 30-34, 90-93, and 95-98 have been rejected under 35 U.S.C. §103 as being obvious over the teachings of Franke *et al.* (*DNA*, 1982, Vol. 1, pages 223-230) in view of Welcher *et al.* (U.S. Patent Application Publication No. 2005/0221344). This rejection is respectfully traversed.

The claims are drawn to isolated polynucleotides encoding the polypeptides consisting of SEQ ID NO:5 or SEQ ID NO:10, or alternatively, SEQ ID NO:10 operably linked to a signal peptide. The polypeptide sequences set forth in SEQ ID NOS:5 and 10 represent carboxy-terminal truncations of human alpha-2b-interferon, wherein the last 8 residues of the human sequence are not present. These truncations are referred to herein as "delta-8" C-terminal truncations of the precursor (SEQ ID NO:5) and mature (SEQ ID NO:10) human alpha-2b-interferon sequences. The claims also recite expression cassettes comprising these isolated polynucleotides, and host cells comprising these expression cassettes. Applicants respectfully submit that the delta-8 C-terminal truncation of the precursor (SEQ ID NO:5) or mature (SEQ ID NO:5) polypeptide for human alpha-2b-interferon is not obvious over the cited prior art for the following reasons.

Franke *et al.* teach production of a delta-11 C-terminal truncation of human alpha-2a interferon, not human alpha-2b interferon, in *E. coli*. See the IFN-αA sequence shown in Figure 1, and contrast it with the human alpha-2b-interferon sequence set forth in of SEQ ID NO:11 of Applicants' Sequence Listing. Franke *et al.* demonstrate that this delta-11 C-terminal truncation has considerably less activity than mature human alpha-2a-interferon as measured in standard

cytopathic effect (CPE) inhibition assays. See Franke *et al.*, at Table 2, page 228, comparing relative specific activity of the delta-11 C-terminal truncation (designated "A-11") with that observed for mature human alpha-2a-interferon, where the values in parentheses are the specific activities as a percentage of that of the native protein. Thus, the A-11 truncation had only 31% and 25% of the specific activity of the native sequence for the CPE inhibition assays on the human amnion WISH cell line and bovine kidney MDBK cell line, respectively. However, Franke *et al.* also note that an alpha-2a-interferon derivative lacking the 13 C-terminal residues "retains nearly all of the anti-viral activity of the intact protein on HeLa and MDBK cells"; see Franke *et al.* at page 228, column 2, lines 20-24.

Thus, Franke *et al.* teach that C-terminally truncated alpha-2a-interferon polypeptides have variable activity that is unpredictable. There is nothing within the teachings of Franke *et al.* to guide one of skill in the art to express a delta-8 C-terminal truncation of the precursor or mature human alpha-2b-interferon polypeptide.

Welcher *et al.* teach rat and human precursor and mature "interferon-like" (IFN-L) polypeptides and discuss possible truncated versions thereof, none of which are a "delta-8" C-terminal truncation of these IFN-L polypeptides. The IFN-L polypeptides taught by Welcher *et al.* share only 33% identity with human alpha-2b-interferon (see the alignment below, comparing the 178-aa mature human IFN-L polypeptide of SEQ ID NO:6 of Welcher *et al.* with the 165-aa mature human alpha-2b-interferon sequence set forth in SEQ ID NO:11 of the present application). As mature human alpha-2a-interferon and mature human alpha-2b-interferon differ by only one residue, this means that the IFN-L polypeptide of Welcher *et al.* also shares only about 33% identity with the mature human alpha-2a-interferon sequence taught by Franke *et al.* Applicants respectfully submit that even if Welcher *et al.* had produced the truncated versions of the human IFN-L polypeptide disclosed therein and assayed for their activity, the results obtained therefore would not reasonably be expected to be applicable to a protein sharing only 33% identity with the human IFN-L polypeptide of SEQ ID NO:6. This is particularly true in view of the unpredictability of C-terminal truncations of human alpha-2a-interferon as taught by Franke *et al.*

Alignment of mature human IFN-L polypeptide of Welcher *et al.* and mature human alpha-2b-interferon

```
#=======================================
#
# Aligned_sequences: 2
# 1: EMBOSS_001
# 2: EMBOSS_001
# Matrix: EBLOSUM62
# Gap_penalty: 10.0
# Extend_penalty: 0.5
#
# Length: 183
# Identity:      60/183 (32.8%)
# Similarity:    77/183 (42.1%)
# Gaps:          23/183 (12.6%)
# Score: 182.0
#
#
#=======================================

EMBOSS_001          1 CNLLNVH---LRRVTWQNLRHLSSMSNSFPVECLRENIAFELPQEFLQYT     47
                      |:|...|   .||    .|..|:.|.......||::...|..|||... .
EMBOSS_001          1 CDLPQTHSLGSRR----TLMLLAQMRRISLFSCLKDRHDFGFPQEEFG-N     45

EMBOSS_001         48 QPMKRDIKKAFYEMSLQAFNIFS-QHTFKYWKERHLKQIQIGLDQQAEYL     96
                      |..|.:.....:||..|.||:|| :.:...|.|..|.:....|.||...|
EMBOSS_001         46 QFQKAETIPVLHEMIQQIFNLFSTKDSSAAWDETLLDKFYTELYQQLNDL     95

EMBOSS_001         97 NQCLEEDENENEDMKEMKENEMKPSEARVPQLSSLELRRYFHRIDNFLKE    146
                      ..|:.:.....| ...|||:            |.|.:|:||.||..:|||
EMBOSS_001         96 EACVIQGVGVTE-TPLMKED-----------SILAVRKYFQRITLYLKE    132

EMBOSS_001        147 KKYSDCAWEIVRVEIRRCLYYFYKFTALFRRK     178
                      ||||.||||:||.||.|.............|.|
EMBOSS_001        133 KKYSPCAWEVVRAEIMRSFSLSTNLQESLRSKE    165
```

Accordingly, Applicants respectfully submit that the combined teachings of Franke *et al.* and Welcher *et al.* fail to suggest Applicants' claimed invention. Reconsideration and withdrawal of this obviousness rejection is therefore requested.

Claims 94 and 99 have been rejected under 35 U.S.C. §103 as being obvious over Franke *et al*. (*DNA*, 1982, Vol. 1, pages 223-230) in view of Welcher *et al.* (U.S. Patent Application Publication No. 2005/0221344) and further in view of Raskin (U.S. Patent No. 6,096,546). This rejection is respectfully traversed.

Claims 94 and 99 are directed to isolated duckweed cells comprising the claimed polynucleotides of the invention. The teachings of Franke *et al.* and Welcher *et al.* are as noted above. Raskin is relied on as teaching expression of proteins in duckweed. However, Applicants respectfully note that Raskin also fails to teach or suggest the claimed polynucleotides encoding delta-8 C-terminal truncations of the precursor and mature human alpha-2b-interferon polypeptides. Thus, while Raskin may teach the suitability of duckweed as a host cell for production of recombinant proteins, it provides no further guidance to one of skill in the art to modify the teachings of Franke *et al.* and Welcher *et al.* to arrive at Applicants' claimed invention. Therefore, reconsideration and withdrawal of this rejection of the claims is respectfully requested.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the rejections of the claims under 35 U.S.C. §103 are now overcome. Accordingly, Applicants submit that this application is now in condition for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby

petitioned under 37 CFR §1.136(a), and any fee required therefore is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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